REMARKS

Claims 14, 17, 19, 23, 24, 26, 27, 29, 32 and 33 remain in the present application.

By way of review, the present invention provides a quick and effective method for assessing whether a patient has suffered axonal damage resulting from a specific group of neurologic traumas (including stroke), and the extent of that damage. Until now, there has been no effective, minimally invasive procedure for quickly determining that information which, of course, can be critical in an emergency room setting. In this method, a patient suspected of having such neurologic trauma, such as a stroke or a blow to the head sustained in a car accident, provides a sample of cerebrospinal fluid. The presence in that fluid of specific tau proteins is then determined using a monoclonal antibody raised against those proteins, and the levels of those proteins in the fluid are compared to control samples representing both damaged and undamaged states. This comparison yields information regarding whether there has been a traumatic head injury and the extent of that injury in the patient.

The Examiner has rejected claim 20, under 35 U.S.C. § 112, second paragraph, based on its use of the phrase "said...tau protein lacks the native N-terminal and C-terminal amino acids". Claim 20 has been canceled herein rendering that rejection moot.

The Examiner has also rejected all claims pending the in the present application, based on the use of the phrase "traumatic head injury" in those claims. The Examiner contends that there is not proper antecedent basis in the present application for the use of that phrase in the claims. Applicant respectfully points out that the phrase "traumatic head injury" has not been used in claim 32, and continues to assert that there is ample antecedent basis in the present application to support use of that phrase. However, in an effort to streamline what is already an overly long prosecution, Applicant has eliminated the use of the phrase "traumatic head injury" in all of the claims and has replaced it with the phrase "neurologic trauma," a phrase that has clear antecedent basis in the present application, at page 5, line 24. Further, Applicant has redefined claim 14, the broadest claim in the present application, such that the described assay is used to assess the presence of damage from acute cerebrovascular accident (another term for "stroke"), primary neuronal injury, primary hemorrhage, primary vascular injury, and secondary traumatic lesions, specific phrases which are all described and exemplified, at page 4, line 17 through page 5, line 4, in the present application. In this light

this, the description of the conditions which the present assay is used to detect are now clearly defined with clear antecedent basis in the present application and, accordingly, the rejection under the first paragraph of 35 USC § 112 should be withdrawn.

Finally, the Examiner has continued his rejection of the claims, under 35 USC § 102(b), contending that they are anticipated by the disclosure of Vandermeeren et al. (WO 94/13795), which deals with the detection of Alzheimer's disease. This rejection is respectfully traversed in view of the amendments to claim 14 herein.

Claim 32 of the present application relates to the use of the assay of the present invention to detect the occurrence and the severity of an acute cerebrovascular accident in a patient. Cerebrovascular accident is a synonym for stroke (see the attached material). Vandermeeren et al. says nothing about the measurement of tau protein in the cerebrospinal fluid of a patient suspected of having a stroke. A similar situation applies to amended claim 14 (and claim 33), which clearly on its face does not encompass the use of the present assay to detect the occurrence or severity of Alzheimer's disease (a chronic condition), but rather deals with the measuring of tau protein in the cerebrospinal fluid of a patient suspected of having suffered a primary neuronal injury, a primary hemorrhage, a primary vascular injury or a secondary traumatic lesion (none of which are taught or suggested in Vandermeeren et al.—and all of which are acute conditions).

The Examiner argues that since Alzheimer's patients inherently are part of the population which have neurologic traumas of the type defined in the claims of the present application, the claimed invention is inherently anticipated by the Vandermeeren et al. disclosure. This is an incorrect reading of the law. Vandermeeren et al. describes the measurement of tau protein in cerebrospinal fluid in patients having Alzheimer's disease. There is nowhere in the Vandermeeren et al. reference that teaches or suggests the measurement of tau protein in the cerebrospinal fluid of a patient who is suspected of having suffered acute cerebral vascular accident, primary neuronal injuries, primary hemorrhages, primary vascular injuries or secondary traumatic lesions of the neurologic system. Thus, there can be no anticipation or obviousness rejection based on the Vandermeeren et al. reference. Even if there is an overlap in the populations between those having Alzheimer's disease and those having, for example, stroke, there is nothing in Vandermeeren et al. that would suggest that if an Alzheimer's patient was suspected of having suffered a stroke, a medical technician

should measure the tau protein in the cerebrospinal fluid of that patient in order to determine whether a stroke had taken place, and the severity of that stroke. To contend otherwise is the use of hindsight in its purest form and is just not supported by Vandermeeren et al. In discussing § 102 inherency rejections, Chisum indicates (at § 3.03[2][b]) that "Federal Circuit decisions emphasize that an anticipatory inherent feature or result must be consistent, necessary and inevitable, not merely possible or probable." There is no way that one can conclude that, based on that disclosure, the testing of an Alzheimer's patient, who happened to have suffered a stroke, for the purpose of measuring the tau protein in that patient's cerebrospinal fluid and thereby determining the extent of that stroke (in spite of the fact that such a connection is nowhere suggested in Vandermeeren et al.) is "consistent, necessary and inevitable," based on the Vandermeeren et al. disclosure. In that regard, the comments in *3M Unitech Corp. v. Ormco Co.*, 96 F Supp 2d 1042, 1047 (2000) are relevant: "It is not sufficient that there is a possibility that something may occur" to demonstrate an inherent anticipation; "occasional results do not show inherency." Even if the tau protein had been measured on an Alzheimer's patient who coincidentally had just recently happened to have a stroke (which would have been a purely fortuitous act), there is nothing in Vandermeeren et al. which would have suggested that those tau protein levels would be indicative of the occurrence or extent of the stroke.

The claims of the present application have now been amended to clearly distinguish them from Vandermeeren et al., which deals solely with Alzheimer's disease. As discussed above, inherency is not an appropriate grounds for rejection under these circumstances. Accordingly, it is respectfully requested that the rejection 35 USC § 102(b), based on Vandermeeren et al., be withdrawn in view of the amendments made to the claims herein.

In light of the foregoing, it is submitted that the currently pending claims in the present application are now in form for allowance. Accordingly, reconsideration and allowance of those claims are earnestly solicited. Applicant has made a good faith effort to address and be responsive to each of the grounds of the rejection made by the Examiner and thereby to place the present application in form for allowance. If any further issues remain, the Examiner is invited to call Applicant's undersigned attorney at the telephone number given below so that those issues can be expeditiously addressed and the present application placed in form for allowance.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that a copy of this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on

July 31, 2003

_____
Sarah Ohlweiler

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After Stroke
Wallace Sife

Restorative Neurology
Larry B. Goldstein

STROKE

Cerebrovascular Accident

A teaching presentation on Stroke

For families patients and rehabilitation team members

Disclaimer: The information presented here is for informational purposes **only**. I take no responsibility for any consequences of anyone interpreting or misinterpreting the information presented here. Always consult your physician if you have any questions.

138543

Posted: April 18th 1996

Medical Encyclopedia

Other encyclopedia topics: A-Ag Ah-Ap Aq-Az B-Bk Bl-Bz C-Cg Ch-Co Cp-Cz D-Di Dj-Dz E-Ep Eq-Ez F G H-Hf Hg-Hz I-In Io-Iz J K L-Ln Lo-Lz M-Mf Mg-Mz N O P-Pl Pm-Pz Q R S-Sh Si-Sp Sq-Sz T-Tn To-Tz U V W X Y Z 0-9

Stroke

Contents of this page:

Illustrations

Brain

Carotid stenosis, X-ray of the left artery

Carotid stenosis, X-ray of the right artery

Circle of Willis

Right cerebral hemisphere - function

Brainstem function

Stroke

Cerebellum - function

Left cerebral hemisphere - function

Endarterectomy

Alternative names *Return to top*

Cerebrovascular disease; CVA; Cerebrovascular accident

Definition *Return to top*

A stroke is when the blood supply to any part of the brain is interrupted, resulting in tissue death and loss of brain function.

Causes and risks *Return to top*

The brain requires about 20% of the body's total circulation of blood. The blood enters the brain from two carotid arteries in the neck, which branch off into multiple arteries that supply each specific area of the brain.

If blood flow in any of these arteries is interrrupted for longer than a few seconds, brain cells can die, causing permanent damage. The resulting stroke-related symptoms depend on the area of the brain affected, the extent of the damage, and the cause of the stroke.

Common symptoms include changes in vision, speech, and comprehension; weakness; vertigo; loss of sensation in a part of the body; or changes in the level of consciousness.

Stroke accounts for 1 out of every 15 deaths in the United States. It is the 3rd leading cause of death in most developed countries, and the leading cause of disability in adults. The risk doubles with each decade after age 35. Stroke occurs in men more often than women.

The risk of stroke is increased by smoking, hypertension, diabetes, hyperlipidemia, and heart disease. Rarely, strokes may happen in women on birth control pills -- the risk is increased if a woman also smokes and is older than 35. Women have a higher risk of stroke during pregnancy and the weeks immediately after pregnancy. Other illnesses such as vasculitis, lupus, or high blood viscosity may contribute to stroke.

The most common cause of stroke is atherosclerosis. (See stroke secondary to atherosclerosis.) Atherosclerosis is a condition in which fatty deposits and blood platelets collect on the wall of the arteries, forming plaques. Over time, the plaques slowly begin to block the flow of blood. A plaque may block the artery enough to cause a stroke, or it may trigger a blood clot that causes a stroke.

The formation of a plaque does not always lead to a stroke. The arteries are large enough that 75% of the blood vessel can be blocked, and there will still be adequate blood flow to that area of the brain. Furthermore, there are many small connections between the arteries in the brain. If the blood flow is gradually blocked in one artery, these small connections will increase in size and "by-pass" the obstructed area. Even a totally blocked artery may not cause a stroke.

A stroke may be caused by a blood clot that forms in the brain (a thrombus) or a blood clot, piece of plaque, or other material that travels to the brain from another location (an embolism). Bleeding (hemorrhage) within the brain can, on rare occassions, cause symptoms that mimic stroke.

A stroke caused by a blood clot in the brain (a thrombus) is most common in older people, and often there is underlying atherosclerosis or diabetes. This type of stroke may occur at any time, including at rest. The person may or may not lose consciousness.

Strokes caused by embolism (a blood clot that travels to the brain) are most commonly caused by heart disorders. An embolism may also originate in the aortic arch, especially where there is atherosclerotic plaque. The blood clot travels through the bloodstream and becomes stuck in a small artery in the brain. This stroke occurs suddenly with immediate, maximum damage to the brain. Consciousness may or may not be lost.

Embolic strokes are NOT associated with activity levels and can occur at any time. Arrhythmias of the heart, such as atrial fibrillation, are often seen with with this type of stroke and may be the cause of the clot. Other causes of embolic stroke include endocarditis (an infection of the heart valves), or a mechanical heart valve that may have a clot attached to it. A heart attack puts people at greater risk for having an embolic stroke.

The probable outcome is worsened if blood vessels damaged by stroke rupture and bleed (hemorrhagic stroke).

See also:

- Stroke secondary to carotid dissection (bleeding from the carotid arteries)
- Stroke secondary to carotid stenosis (narrowing of the carotid arteries)
- Stroke secondary to cocaine
- Stroke secondary to FMD (fibromuscular dysplasia)
- Stroke secondary to syphilis

Prevention *Return to top*

Stroke prevention involves controlling the risk factors. Treat hypertension, diabetes, heart disease, and other associated disorders. Reduce or stop smoking. A low-cholesterol, low-salt diet may be appropriate if the risk factors include atherosclerosis or hypertension. Exercise more.

The treatment of TIA can prevent some strokes.

Symptoms *Return to top*

- Loss of movement (paralysis) of any body area
- Weakness
- Decreased sensation
- Numbness
- Tingling or other sensation changes
- Decreased vision
- Language difficulties (aphasia):
    - slurred, thick, difficult speech
    - inability to speak
    - inability to understand speech
    - may have difficulty with reading or writing
- Inability to recognize or identify sensory stimuli (agnosia) resulting in "neglect" of one side of the body
- Loss of memory
- Vertigo (abnormal sensation of movement)
- Loss of coordination
- Swallowing difficulties
- Personality changes
- Mood/emotion changes (such as depression or apathy)
- Consciousness changes:
    - sleepy
    - stuporous/somnolent/lethargic
    - comatose/unconscious
- Urinary incontinence (lack of control over bladder)
- Lack of control over the bowels
- Cognitive decline
    - dementia
    - easily distracted
    - impaired judgment
    - limited attention

Additional symptoms that may be associated with this disease:

- Tongue problems
- Seizures
- Movement, unpredictable - jerky
- Movement, uncontrollable
- Movement, dysfunctional
- Incontinence
- Fatigue
- Fainting
- Facial paralysis

- Eye movements, uncontrollable
- Eye lid drooping
- Drooling
- Breathing, absent temporarily
- Behavior, unusual or strange
- Abnormal lack of sweating

Note: Specific changes in brain function (neurologic deficits) depend on the location and amount of injury to the brain. The symptoms are typically on one side of the body but may be isolated to specific functions, may involve one side of the body and the opposite side of the face, or may involve the face only.

Signs and tests *Return to top*

In diagnosing a stroke, the way the symptoms develop is important. The symptoms may be severe at the beginning of the stroke, or symptoms may progress or fluctuate for the first day or two (stroke in evolution). Once there is no further deterioration, the stroke is considered a complete stroke.

The exam will look for specific neurologic, motor, and sensory deficits, because these often correspond closely to the location of the injury to the brain. An examination may show changes in vision or visual fields, abnormal reflexes or abnormal extent of "normal" reflexes, abnormal eye movements, muscle weakness, decreased sensation, and other changes. A "bruit" (an abnormal sound heard with the stethoscope) may be heard over the carotid arteries of the neck. There may be signs of atrial fibrillation.

Tests may determine the location and cause of the stroke and rule out other disorders that can cause the symptoms:

- A head CT or MRI of head may be used to rule out bleeding (hemorrhage) or other lesions and define the location and extent of the stroke
- An ECG (electrocardiogram) may be used to determine underlying heart disorders
- An echocardiogram may be used if the cause is suspected to be cardiac embolus
- A carotid duplex (ultrasound) may be used if the cause is suspected to be carotid artery stenosis
- A cerebral (head) arteriography may be used if a disorder involving the blood vessels is suspected

This disease may also alter the results of the following tests:

- Platelet aggregation test
- Osmolality
- LDH isoenzymes
- LDH
- Cytometric study
- CSF collection
- CPK isoenzymes
- BERA (brainstem evoked response audiometry)

Treatment *Return to top*

A stroke is serious condition. Immediate treatment is required. The treatment varies depending on the severity of symptoms. For virtually all strokes, hospitalization is required, possibly including intensive care and life support.

There is no known cure for a stroke. The treatment involves rehabilitation (based on the symptoms) and prevention of future strokes. Recovery may occur as other areas of the brain take over functioning for the damaged areas. The goal of treatment is to prevent the spread of the stroke and to maximize the patient's ability to function.

IMMEDIATE TREATMENT

Life support and coma treatment are performed as needed.

A number of medications may be used. RTPA is a medicine that lyses the clot and potentially restores blood flow to the affected area to prevent cell death and permanent damage. However, there are strict criteria for who can receive RTPA -- most important is that the stroke victim be evaluated and treated by a specialized stroke team within 3 hours of onset of symptoms. It is a controversial medication because there is a risk of serious bleeding.

In appropriate circumstances, other anti-coagulants such as heparin and coumadin are used to prevent recurrent strokes. Aspirin and other anti-platelet agents are used to prevent strokes as well.

Analgesics may be needed to control severe headache. Anti-hypertensive medication may be needed to control high blood pressure.

Nutrients and fluids may be neccesary, especially if the person has swallowing difficulties. The nutrients and fluids may given through an intravenous tube or a tube in the stomach (feeding tube or gastrostomy tube). Swallowing difficulties may be temporary or permanent.

Surgery may be appropriate in some cases, including surgical removal of blood clots from the brain.

Carotid endarterectomy, removal of plaque from the carotid arteries, may help prevent new strokes from occurring in some people.

LONG-TERM TREATMENT
The recovery time and need for long-term treatment vary. Depression and other symptoms should be treated.

Speech therapy, occupational therapy, physical therapy, positioning, range of motion exercises, and other therapies may prevent complications and promote maximum recovery of function. People should stay active within their physical limitations.

In some cases, urinary catheterization or bladder/bowel control programs may be necessary to control incontinence.

The individual's safety must be considered. Some people with stroke appear to have no awareness of their surroundings on the affected side. Others show a marked indifference or lack of judgment, which increases the need for safety precautions. For these people, friends and family members should repeatedly reinforce important cues, like name, age, date, time, and where they live, to help reduce disorientation.

Communication may require pictures, demonstration, verbal cues, or other strategies, depending on the type and extent of language deficit.

In-home care, boarding homes, adult day care, or convalescent homes may be required to provide a safe environment, control aggressive or agitated behavior, and meet physiological needs.

Behavior modification may be helpful for some people in controlling unacceptable or dangerous behaviors. This consists of rewarding appropriate or positive behaviors and ignoring inappropriate behaviors (within the bounds of safety).

Family counseling may help in coping with the changes required for home care. Visiting nurses or aides, volunteer services, homemakers, adult protective services, and other community resources may be helpful.

Legal advice may be appropriate. Advance directives, power of attorney, and other legal actions may make it easier to make ethical decisions regarding the care of the person with organic brain syndromes such as stroke.

Support groups *Return to top*

American Stroke Association
A Division of the American Heart Association
7272 Greenville Avenue, Dallas, TX 75231
http://www.strokeassociation.org

Toll free phoneline for stroke survivors and caregivers: 1-888-4STROKE

Prognosis *Return to top*

Stroke is the third leading cause of death in developed countries. The outlook depends on the cause and extent of damage. Of those who survive a stroke, many have long-term disabilities, but some recover most or all function.

Complications *Return to top*

- Pressure sores
- Permanent loss of movement or sensation of a part of the body
- Bone fractures
- Joint contractures
- Muscle spasticity
- Permanent loss of cognitive or other brain functions
- Disruption of communication, decreased social interaction
- Decreased ability to function or care for self
- Decreased life span
- Multi-infarct dementia
- Side effects of medications
- Aspiration
- Malnutrition
- Pain syndromes (reflex sympathetic dystrophy)

Call your health care provider if *Return to top*

Go to the emergency room or call the local emergency number (such as 911) if you have symptoms of a stroke. Stroke requires immediate treatment.

Update Date: 01/30/01

Updated by: Galit Kleiner-Fisman, MD, Beth-Israel Deaconess Medical Center, Boston, MA. Review provided by VeriMed Healthcare Network.

Illness

Health Care Information Resources ... for patients, their families, friends and health care workers

The address of this page is: http://hsl.mcmaster.ca/tomflem/stroke.html

Cerebrovascular Accident Links

For more information, see: *Aphasia*, also in the Illness section of this resource.
For more information, see: *Heart disease*, also in the Illness section of this resource.
For more information, see: *Heart health* in the Wellness section of this resource.

- Cerebrovascular accident - Stroke Information Guide from the U.S. NINDS
- Cerebrovascular accident - Heart & Stroke *A-Z* Guide from the American Heart Association
- Cerebrovascular accident - Heart and Stroke Foundation of Canada reducing the toll of disability and death
- Cerebrovascular accident - Heart and Stroke Foundation of Alberta & NWT fighting Canada's number one killers
- Cerebrovascular accident - Nebraska Stroke Foundation basic information on stroke and rehabilitation
- Cerebrovascular accident - Institute For Reparative Medicine and Vascular Surgery heightening awareness of stroke
- Cerebrovascular accident - StrokeCenter from the Washington University School of Medicine, in St. Louis, MO
- Cerebrovascular accident - A Strike Against Stroke an article from *Scientific American*
- Cerebrovascular accident - Take Wellness to Heart about heart disease & stroke in women, from the AHA
- Cerebrovascular accident - NI MAST consensus statement on medical management of stroke
- Cerebrovascular accident - Northern Ireland Chest Heart & Stroke Assocation rehabilitation and prevention
- Cerebrovascular accident - Stroke Prevention Council stroke education for Southern California communities
- Cerebrovascular accident - Rehabilitation for Strokes Japanese-inspired English, but understandable, valuable insights
- Cerebrovascular accident - Stroke and Aging Research Project Bibliography from Columbia-Presbyterian Medical Center
- Cerebrovascular accident - American Stroke Association a division of the *American Heart Association*
- Cerebrovascular accident - National Stroke Association reducing the impact and the incidence of stroke
- Cerebrovascular accident - StrokeHelp.com practical therapeutic suggestions for those helping stroke survivors
- Cerebrovascular accident - Stroke Information Directory fact sheets, testing primers, clinical guidelines, and more

Please read.